

**NIDA Blending Meeting**  
**Smoking Cessation Workshop**  
March 15, Grand Hyatt, New York, NY.

**Nicotine Dependence Among  
Substance Abusing Populations**

- The Epidemiology, Neurobiology, and Treatment of Nicotine Dependence
- Interaction of Nicotine and Cigarette Smoking With Substance Abuse
- Practical and Research Experience of Smoking Cessation in Drug Rehabilitation Programs

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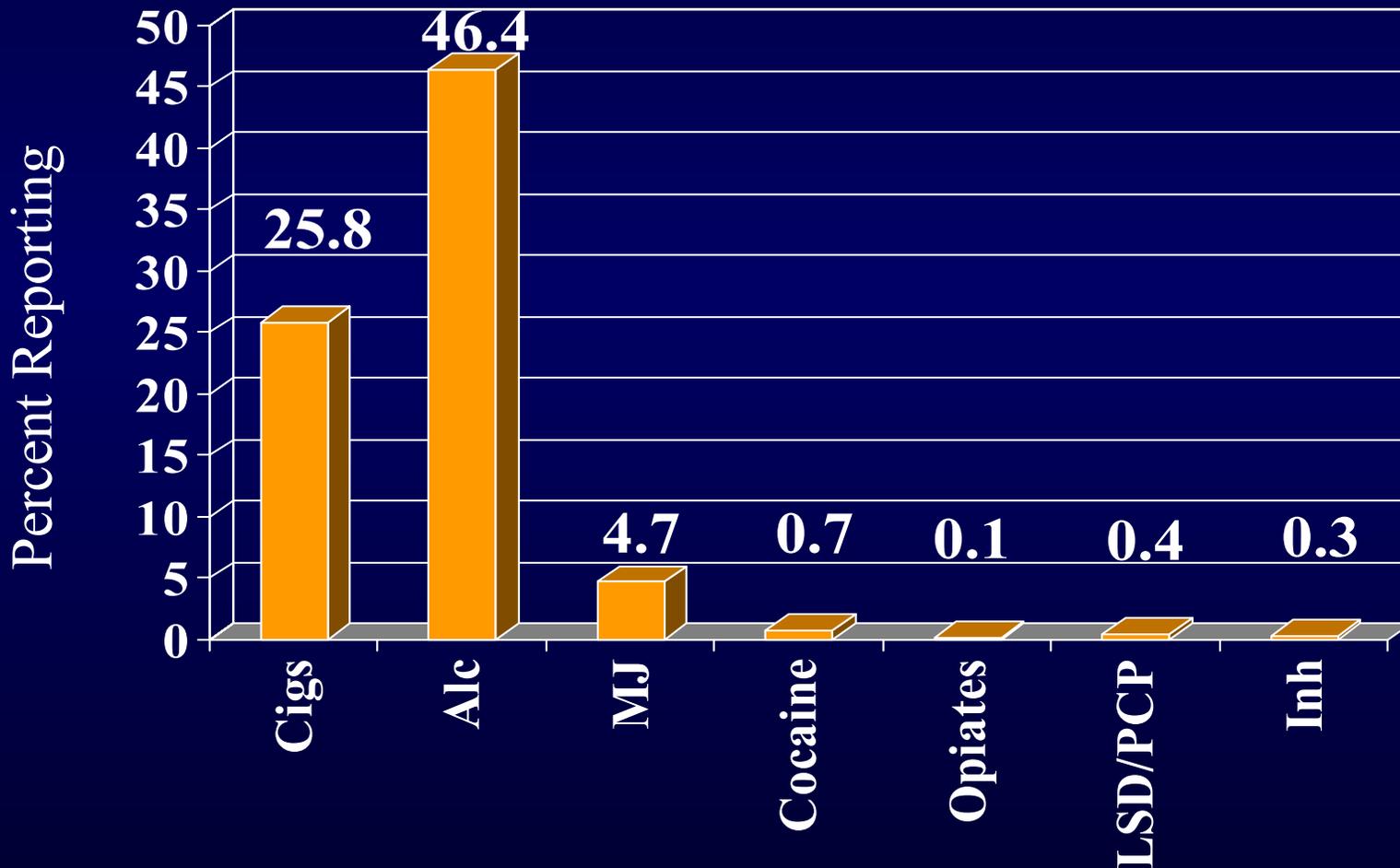
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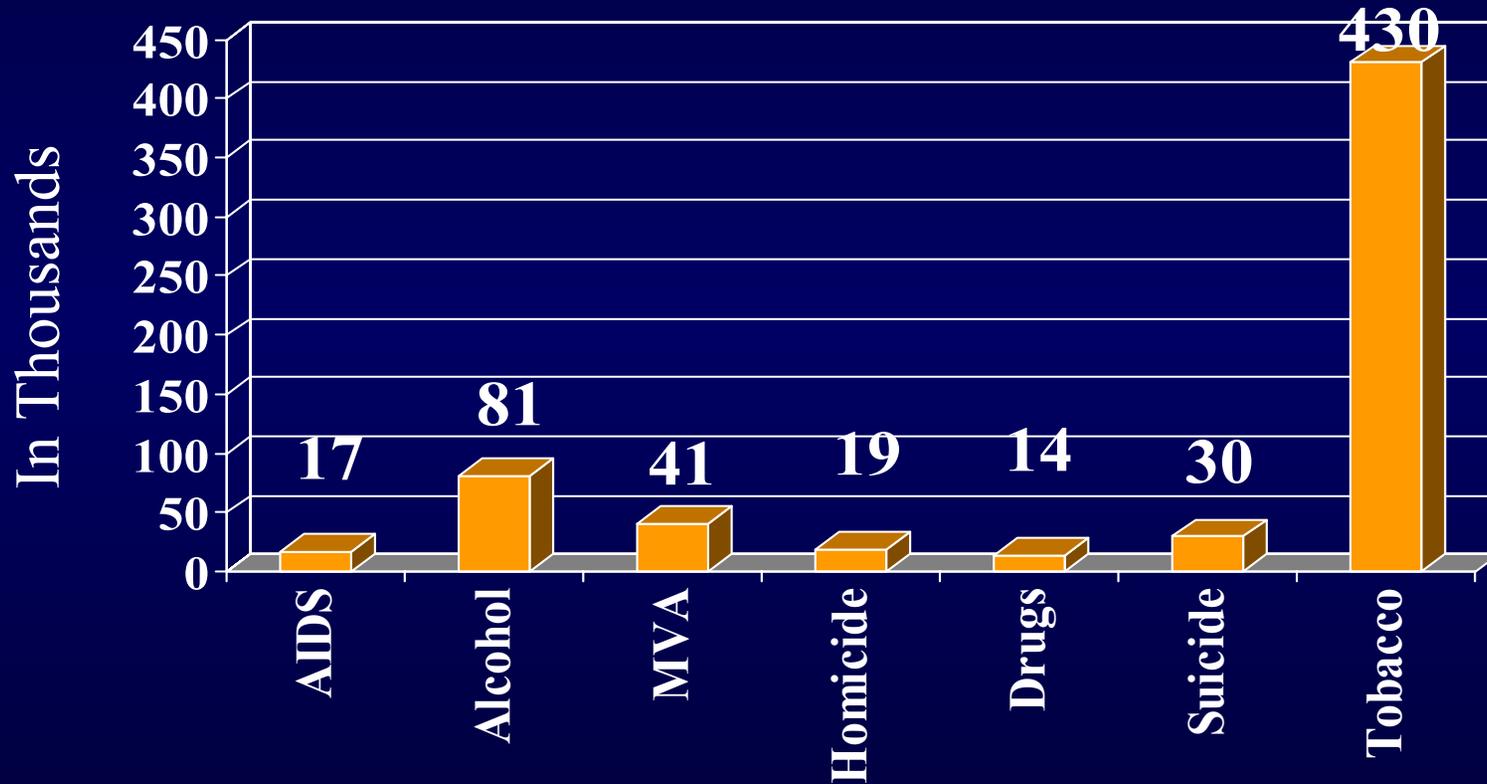
# General Classes of Drugs

- Sedative/barbs – alcohol, benzodiazepines, GHB?
- Stimulants – cocaine, speed, nicotine
- Opiates – heroin, percodan, dilaudid, vicodin
- Hallucinogens – LSD, mescaline, peyote
- Tranquilizers – ketamine, PCP
- Cannabinoids – pot, hash
- Inhalants - poppers

# Substance Use Past Month: NHSDA, 2000



# Mortality and its Causes: 2000



CDC, 2000: <http://www.cdc.gov>

# Important Tobacco and Drug-Related Concepts

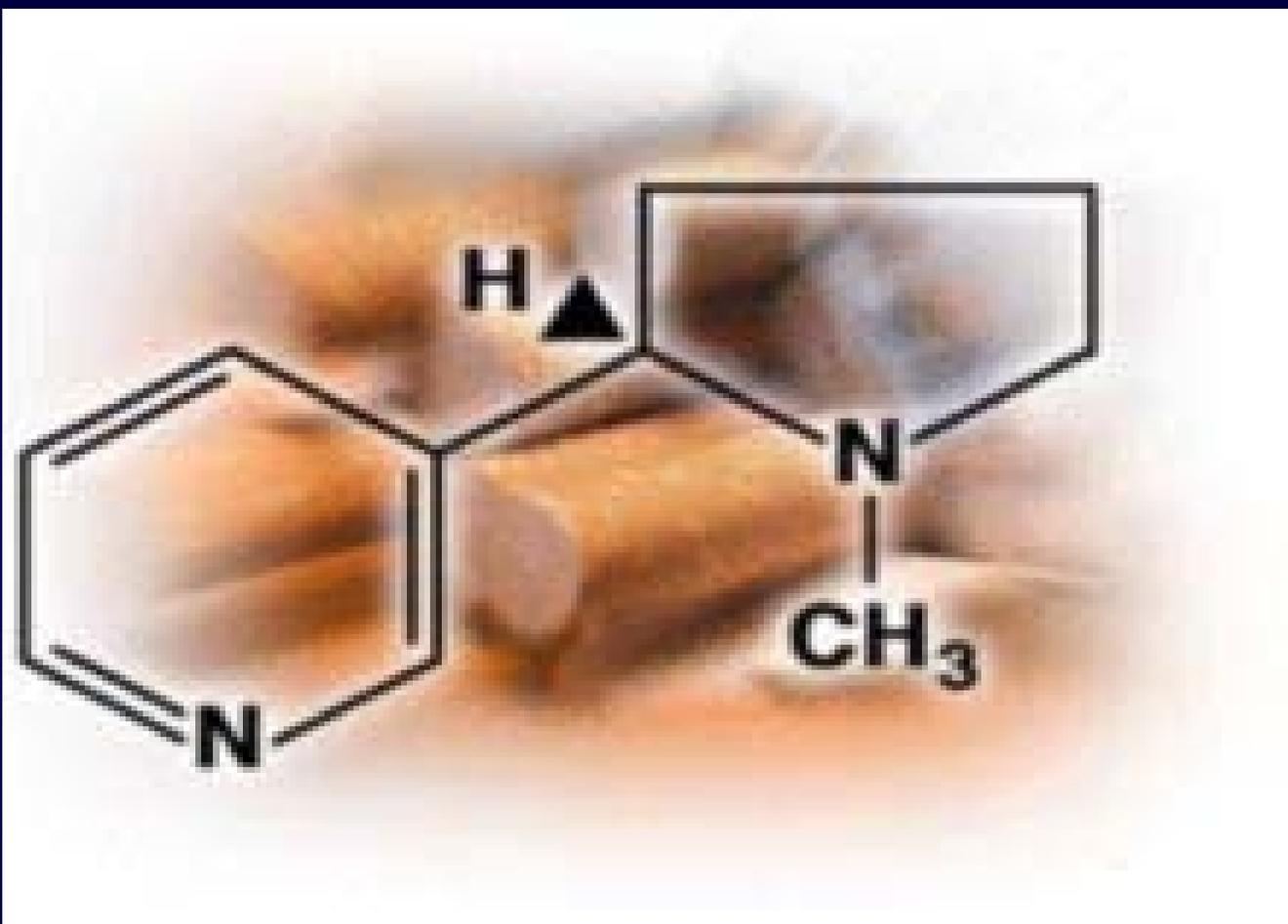
- Addiction Potential – correlated with speed drug gets to reward centers in the brain
  - Route of Administration
- Gateway Hypothesis – most heroin users smoke cigarettes, but few cigarette smokers use heroin
- Drug dependence is a chronic, relapsing condition. Multiple treatments usually needed before abstinence is achieved
- Motivation should not be used as titer for treatment

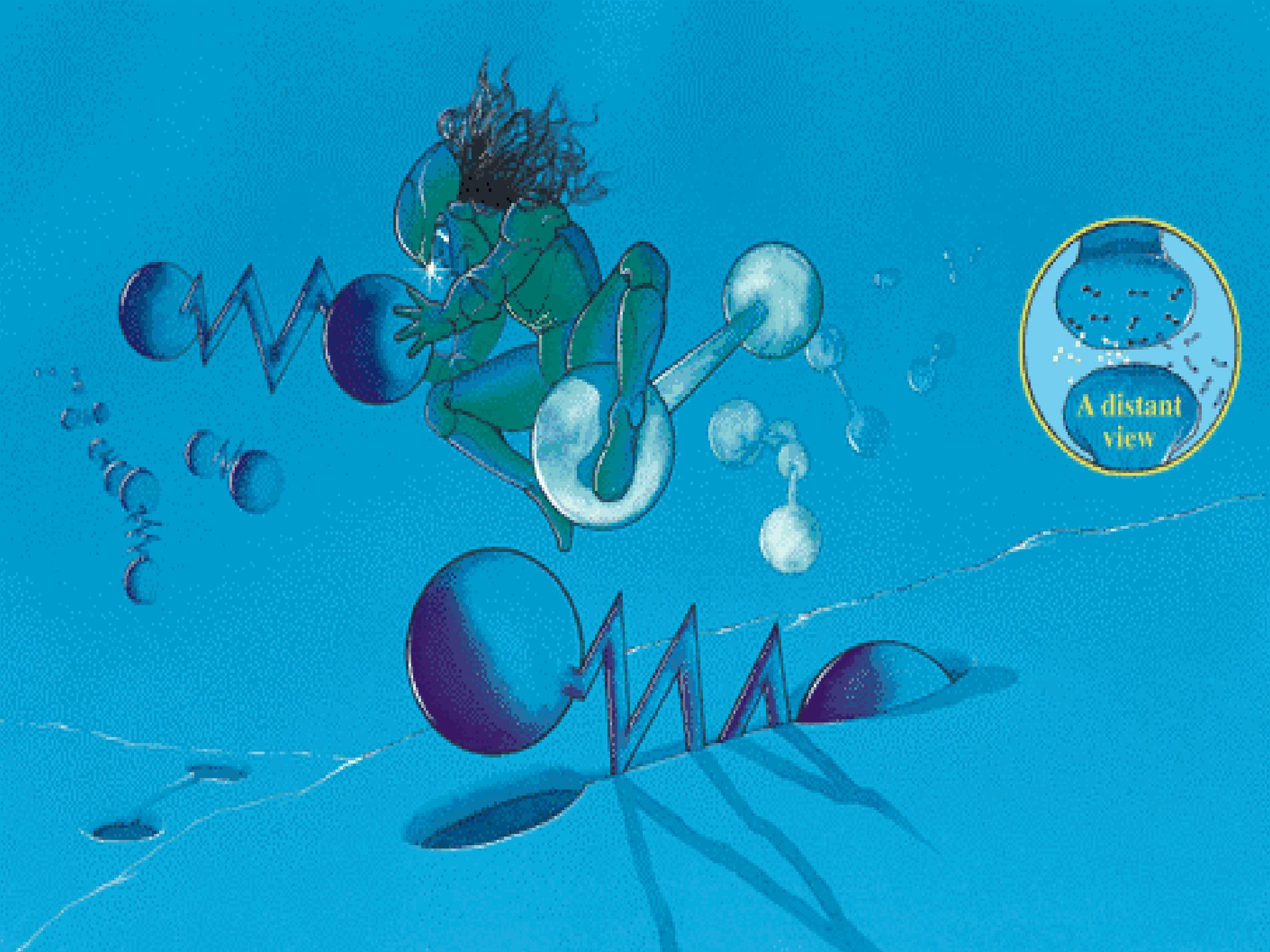




# Important Neurobiology Concepts

- Billions of nerve cells in brain that communicate using neurotransmitters
- Neurons have receptors that accept uniquely shaped molecules to “transmit” a message
- Nicotine is shaped much like the neurotransmitter acetylcholine (ACH)
- Substances also act at neurotransmitter sites
- Nicotine and other substances cause psychoactive effects





A distant view

Nerve Ending  
Containing  
Acetylcholine  
Sacs

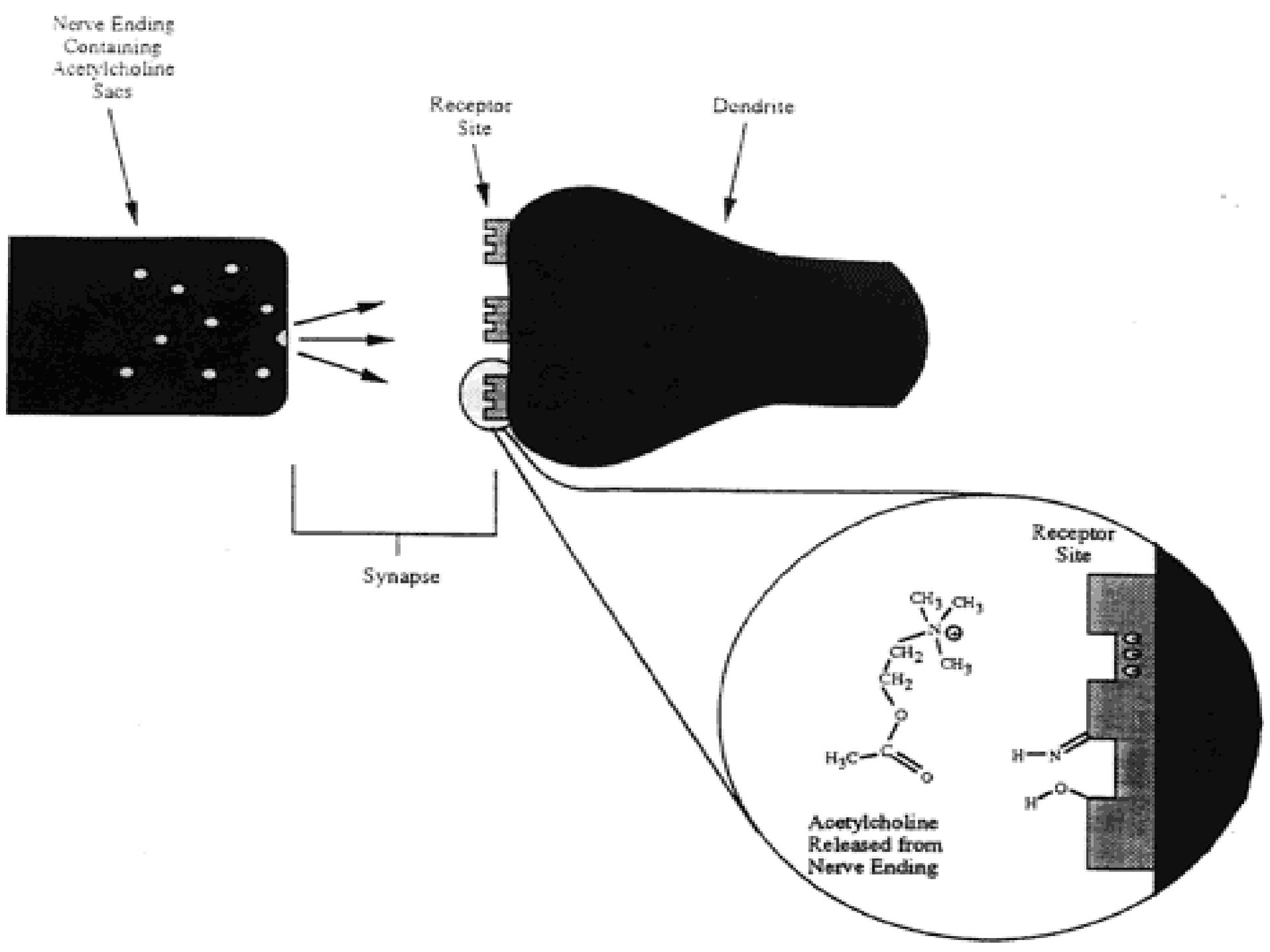
Receptor  
Site

Dendrite

Synapse

Receptor  
Site

Acetylcholine  
Released from  
Nerve Ending



# Nicotine Effects on Brain

- Activity is mediated through responsiveness at nicotinic ACH receptors throughout brain (Plowchalk and deBethizy, 1992)
- Causes desynchronization of EEG (arousal) (Armitage et al., 1968; Remond et al., 1979)
- Serves as a positive reinforcer (Dursun and Kutcher, 1999)

# Rewarding Effects of Nicotine

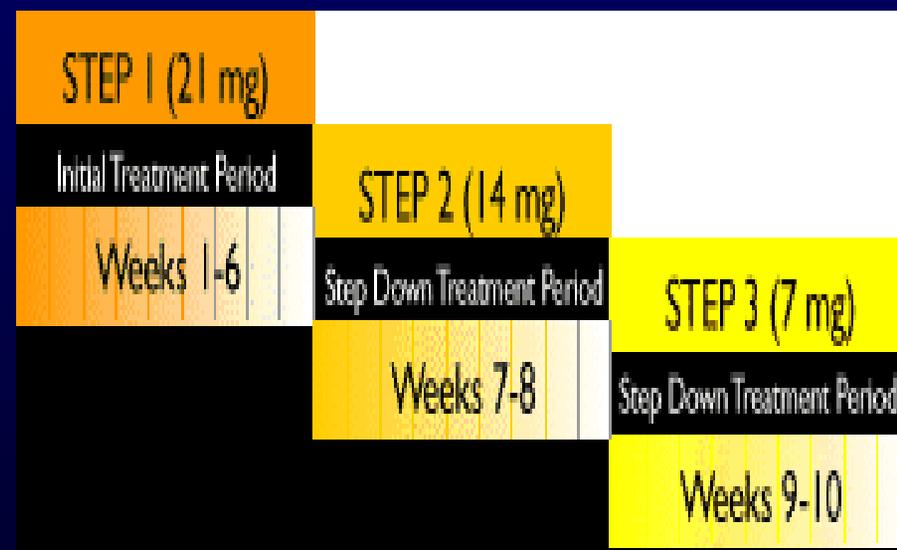
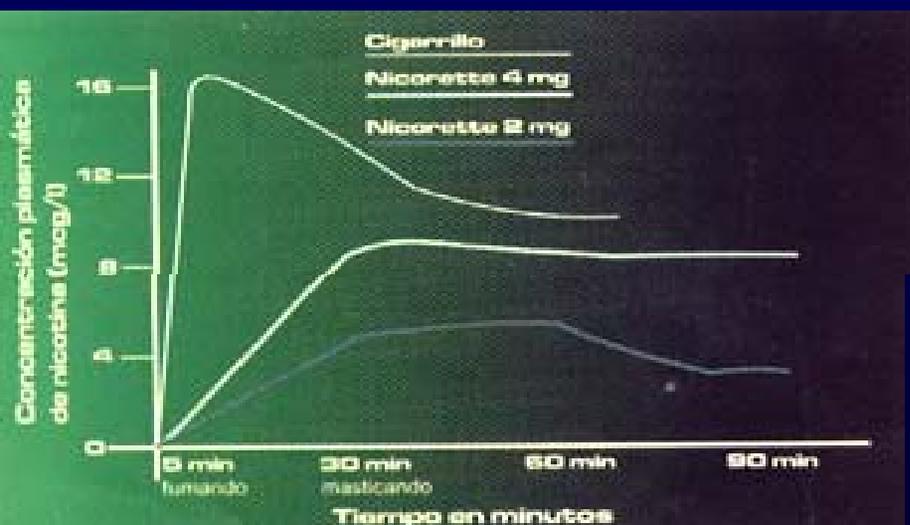
- Rewarding effects mediated via activation of mesolimbic dopamine system (Sing et al., 1982), a common neural substrate for all addictions
- Rewarding (Goldberg et al., 1981) and stimulatory effects (Reid et al., 1998) strongly influenced by environmental factors
- Also serves as potent aversive stimulant at high doses and with non-habituated individuals.

# Smoking Cessation Treatments

- Pharmacotherapy
- Behavioral Therapies
- Self-Help

# Pharmacotherapy Effectiveness

- **Nicotine Gum: 16.0%** (Viswesvaran & Schmidt, 1992; Tonnesen et al., 1988)
- **Nicotine Patch: 22.0%** (Fiore et al., 1994)
- **Zyban: 18.4%** (Jorenby et al., 1999)







# Pharmacotherapy Guidelines

- Clinician familiarity with medications
- Contraindications for the patient
- Patient preference
- Previous experience (pos or neg)
- Patient characteristics (concerns about weight gain; depression history)

# Brief Interventions – Five “A”s

- Ask about tobacco use
- Advice to quit
- Assess willingness to quit
- Assist with the quit attempt
- Arrange for follow-up

# Behavioral Interventions

- Freedom from Smoking: Psychoeducation, positive reinforcement, anxiety reduction
- Fresh Start: Psychoeducation, positive reinforcement, anxiety reduction
- Mood Management (Hall et al., 1997): Psychoeducation, cognitive behavioral strategies, positive reinforcement

# Phenomenology: Smokers Dependent on other Substances

- Smoke a lot; many want to quit
- Social contexts reinforce smoking
- Have many negative health consequences
- Gain from consistent treatment messages
- Reinforcing to quit smoking

Susman, 2000

# Dual-Treatment Drawbacks

- Low success rate (Hurt et al., 1993)
- Quitting smoking interferes with outcomes for other substances (?)
- Few negative immediate consequences to smoking (Kalman, 1998)
- Psychological factors support smoking

# Substance Abusers who Smoke:

- Began smoking at earlier age (Orleans et al., 1993)
- More addicted to nicotine
- Have more cognitive deficits and psychological problems (Burling et al., 1997)
- Have more medical problems (Susman, in press)

# Associations Between Nicotine and Abused Substances

- Cocaine and nicotine high: synergism and substitute for each other reported in cocaine users (Sees, 1993)
- Crack cocaine and tobacco smokers exposed to cocaine cue: enhanced cocaine craving
  - Nicotine patch enhanced cocaine craving
  - Nicotine blocker, mecamylamine, reduced cocaine craving (Reid et al., 1998, 1999)
- In animals: Mecamylamine inhibited alcohol drinking (Ericson et al, 1998), Nicotine enhanced cocaine self-administration (Horger et al., 1992).

# Smoking and Stimulants

- Among healthy smokers, rate of cigarette smoking increased following an injection of cocaine (Nemeth-Coslett et al., 1986) or amphetamine (Low et al, 1984)
- Among cocaine dependent smokers, urine cotinine was higher on days when urine samples also indicated recent cocaine use (Roll et al., 1997)

# Smoking and Alcohol

- Strong association between alcohol use and smoking in general population  
(Craig & Van Natta, 1977)
- Strong predictor of relapse in self-quitters is alcohol use  
(Ockene, 2000)
- Among alcoholics in treatment, about half are interested in smoking cessation  
(Joseph, 1993)
- No data that smoking cessation degrades outcomes for substance treatment

# Smoking and Methadone

- Methadone dose increases associated with increased smoking; Methadone dose decreases associated with decreased smoking (Schmitz et al., 1994)
- Methadone self-administration (up to 10 ml) highest for nicotine 4mg gum, moderate for 2mg gum, lowest for placebo (Spiga et al., 1998)

# Smoking Cessation in Methadone Maintenance

- Prevalence of smoking in methadone maintained between 85%-98%
- Clinical trial of relapse prevention, contingency management (alone and in combination) for optimizing outcomes using nicotine replacement therapy

Acknowledgements: NIDA 1 R01 DA 09992 and GlaxoSmithKline

# Method

- 175 Subjects received NRT and randomly assigned to 1 of 4 conditions for 12 weeks
  - 8 weeks at 21 mg
  - 2 weeks at 14 mg
  - 2 weeks at 7 mg
- Relapse prevention – weekly group
- Contingency management - \$447 max

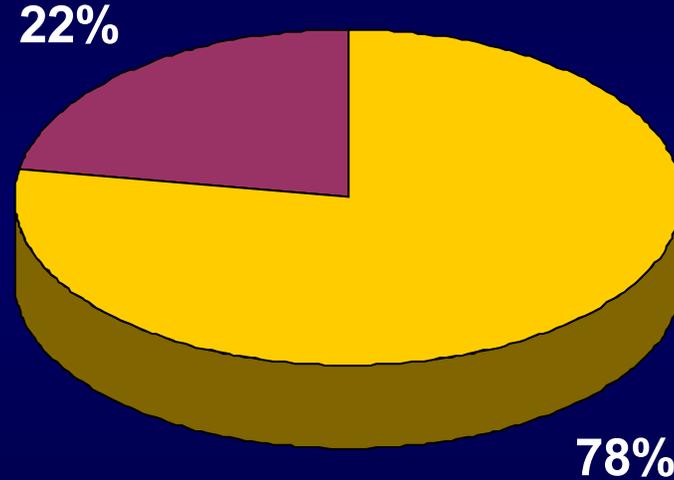
## Method (Cont'd)

- Urine and breath collection on Mondays, Wednesdays, Fridays; Follow-up assessments at 6- and 12-months
- Carbon monoxide criteria indicating smoking abstinence was 8 ppm

# Results

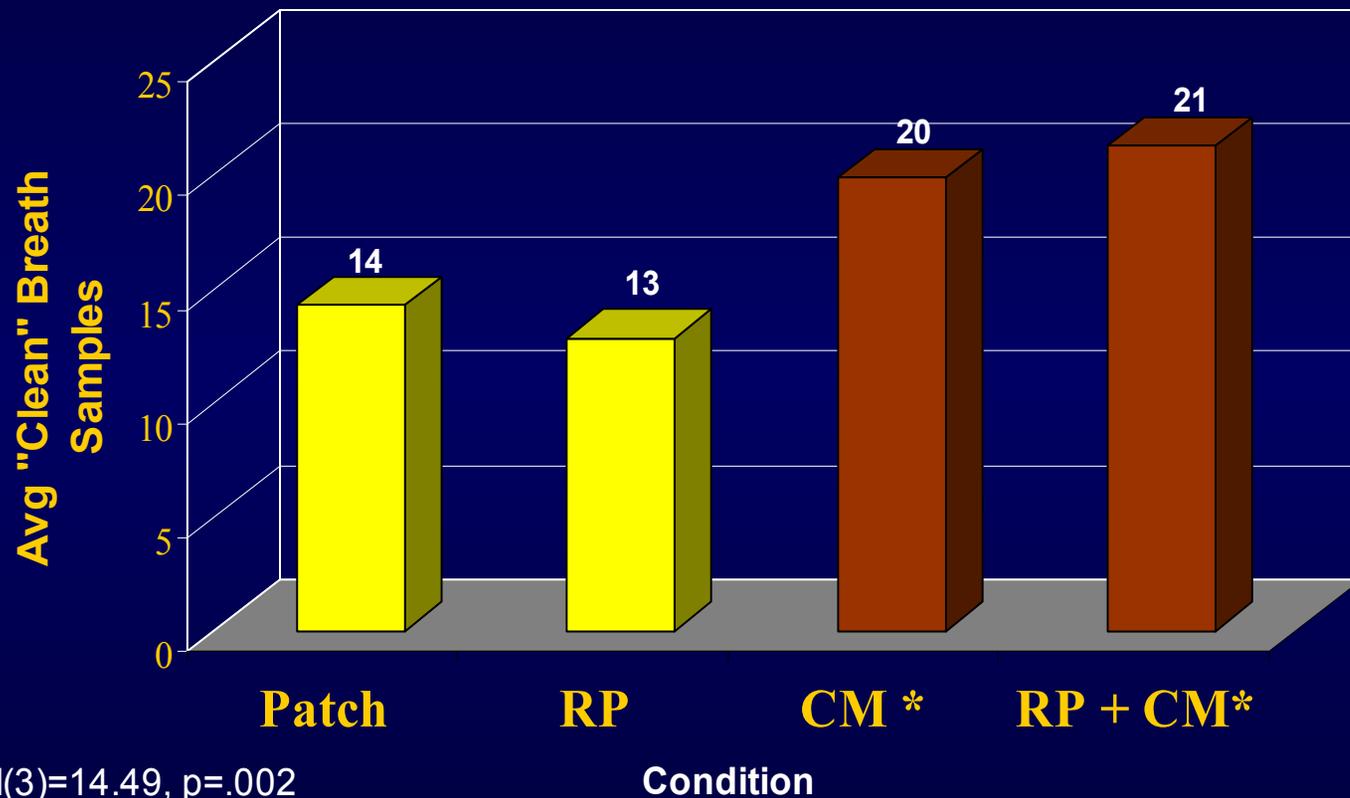
- 73.1% completed 12 weeks of treatment
- Subjects receiving CM showed higher rates of smoking abstinence during the trial than those not assigned to CM ( $p=.0003$ ); no similar effect for RP
- No significant differences in smoking abstinence at 6- and 12-month follow-ups

# Percentage of Smokers vs. Non-Smokers after 12 Weeks of Treatment

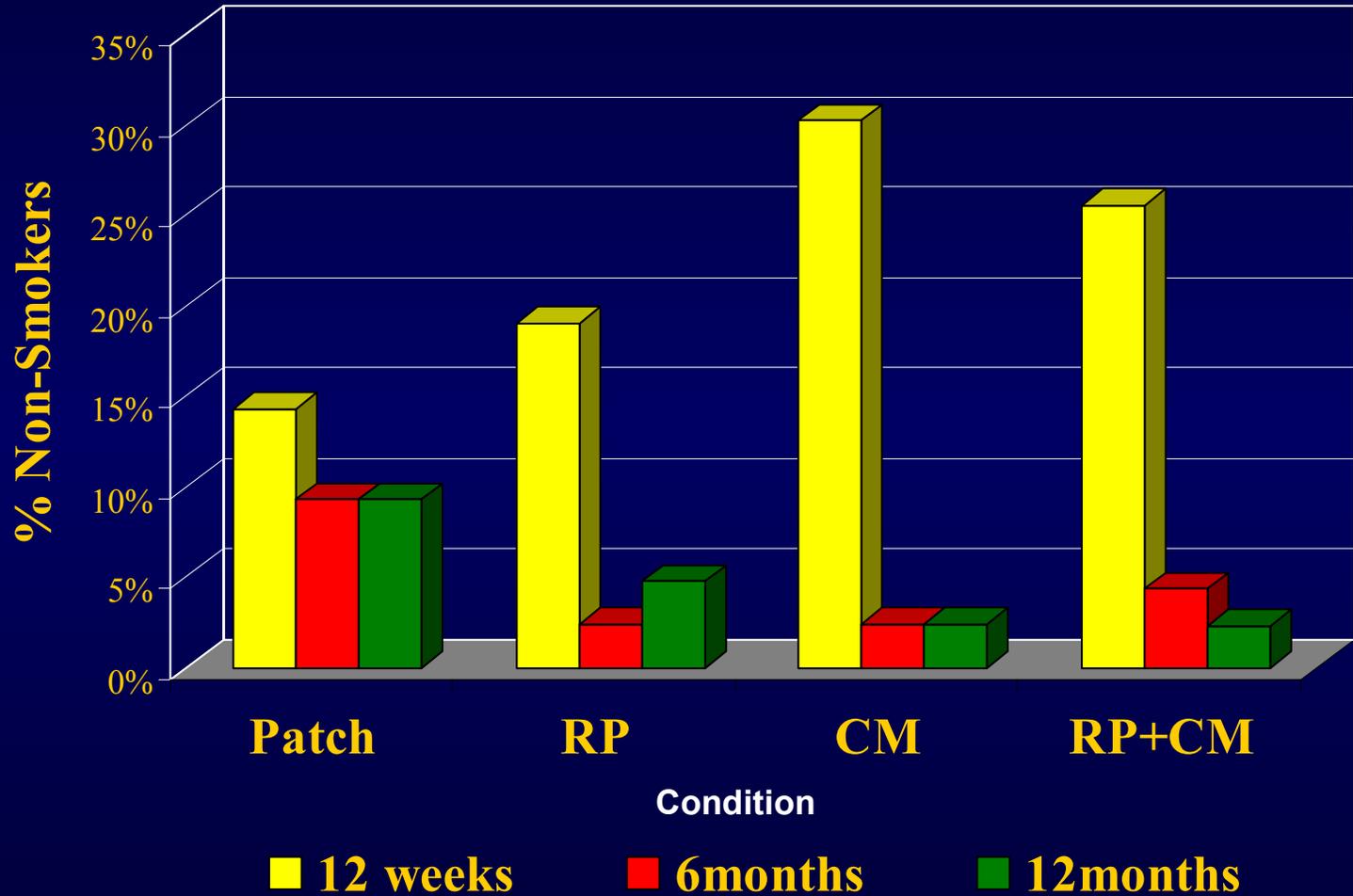


■ Smokers ■ Non-Smokers

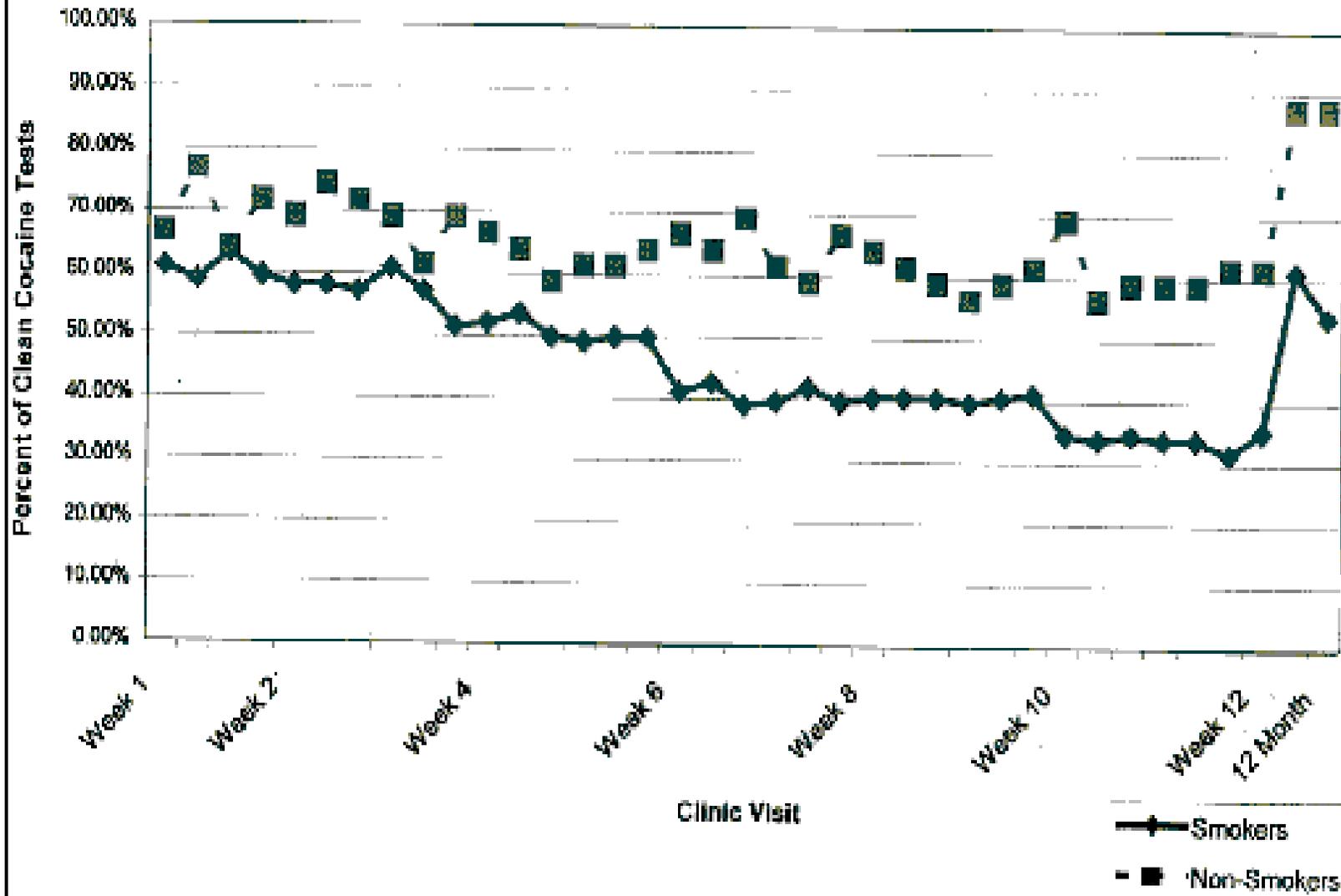
# Effect of Contingency Management on CO During Treatment



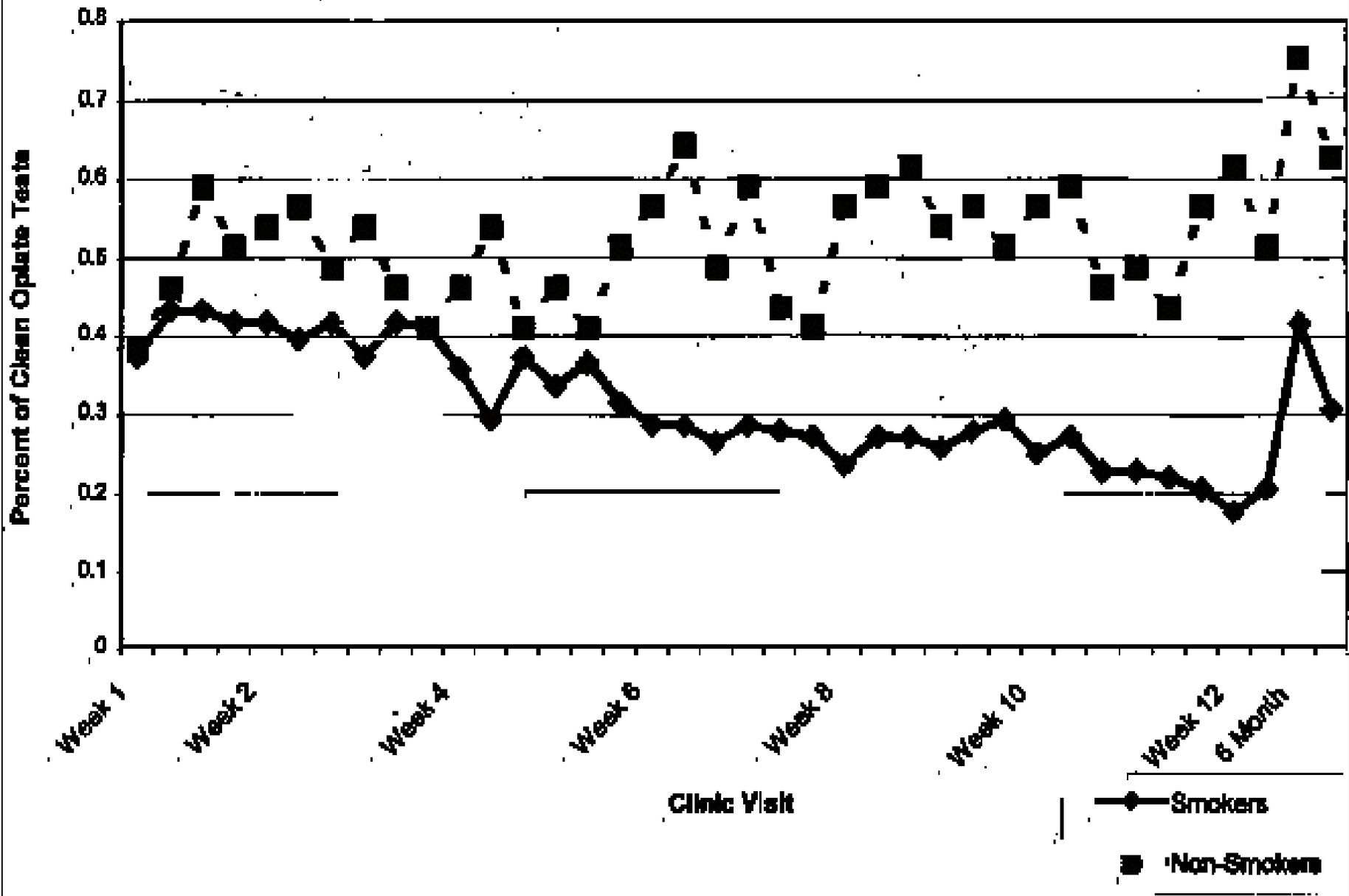
# Confirmed Non-Smokers by Condition



### Percent of Clean Cocaine Samples Provided by Smokers and Non-Smokers



# Percent of Clean Oplate Samples Provided by Smokers and Non-Smokers



# Results

- Subjects provided more opiate and cocaine-free urine samples during weeks when they met criteria for smoking abstinence than during weeks when they did not meet these criteria

# Conclusions

- Contingency management optimized smoking cessation outcomes using NRT during treatment for opiate dependence
  - Effects not maintained
- Strong associations between reductions in cigarette smoking and reductions in illicit drug use during treatment

# **Prospective Study of Illicit Drug Use and Smoking**

- **Seven consecutive days of urine samples, analyzed for metabolites of nicotine, heroin, and cocaine**
- **Concurrent collection of expired carbon monoxide**
- **Detailed smoking history**

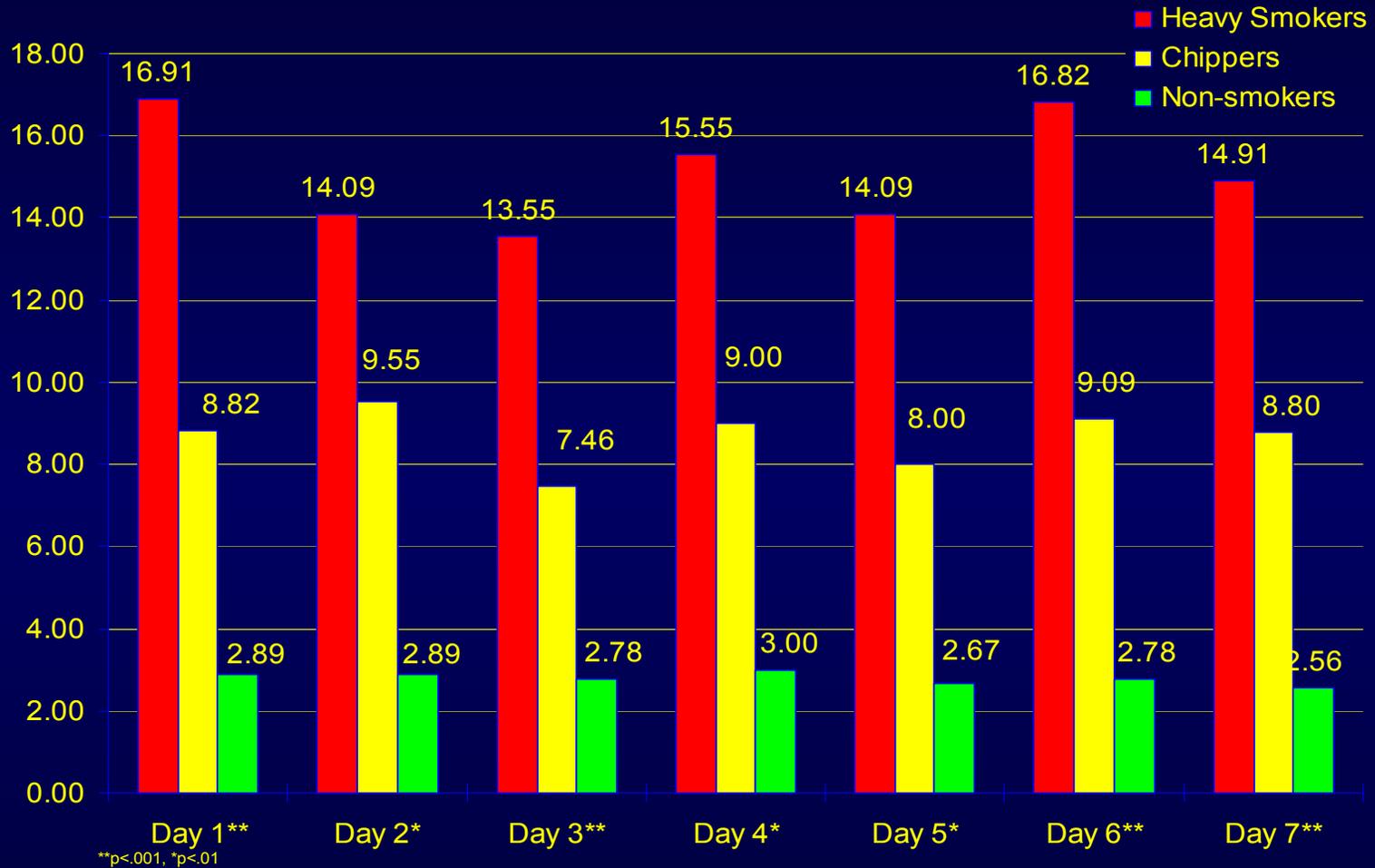
Frosch et al., 2001

# Participant Demographics

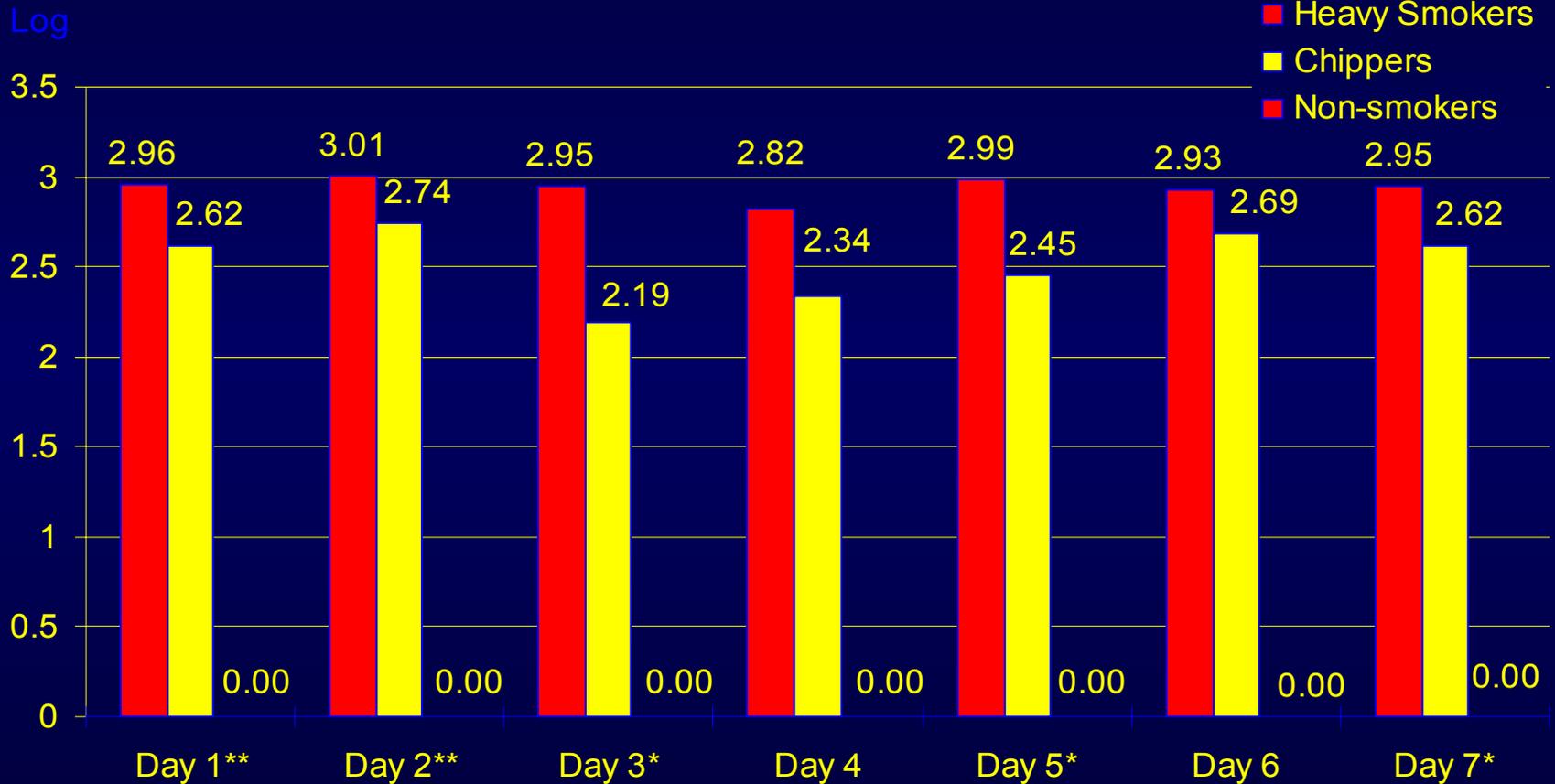
	<b>Heavy Smokers (n=11)</b>	<b>Chippers (n=11)</b>	<b>Non- Smokers (n=9)</b>
<b>Age</b>	<b>40.18 (4.83)</b>	<b>43.36 (8.14)</b>	<b>46.00 (12.49)</b>
<b>% Female</b>	<b>72.7</b>	<b>72.7</b>	<b>55.6</b>
<b>% Hispanic</b>	<b>81.8</b>	<b>63.6</b>	<b>33.3</b>

# Carbon Monoxide Levels by Smoking Status

Daily Expired CO Values

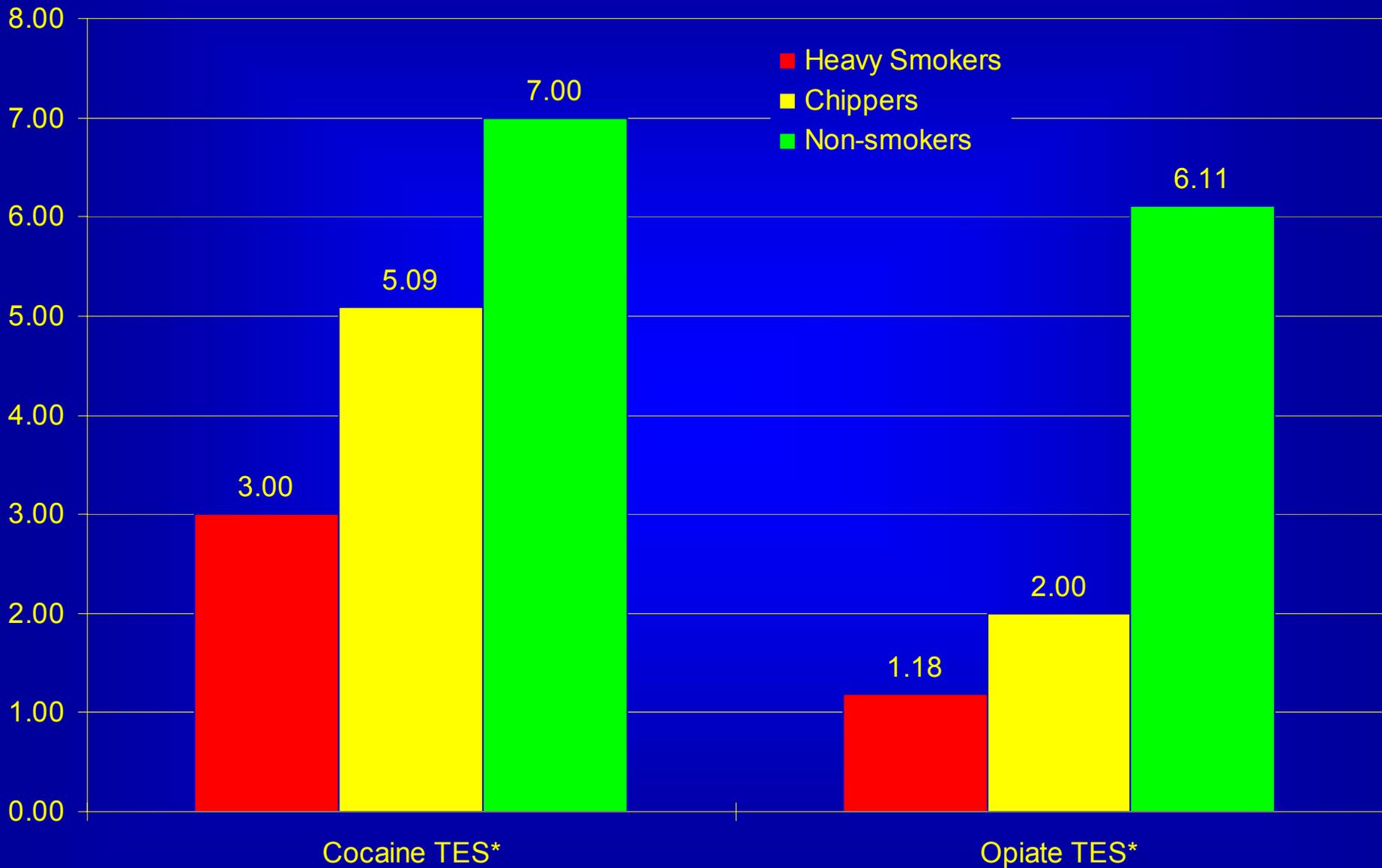


# Daily Urine Cotinine Concentrations Adjusted for Creatinine



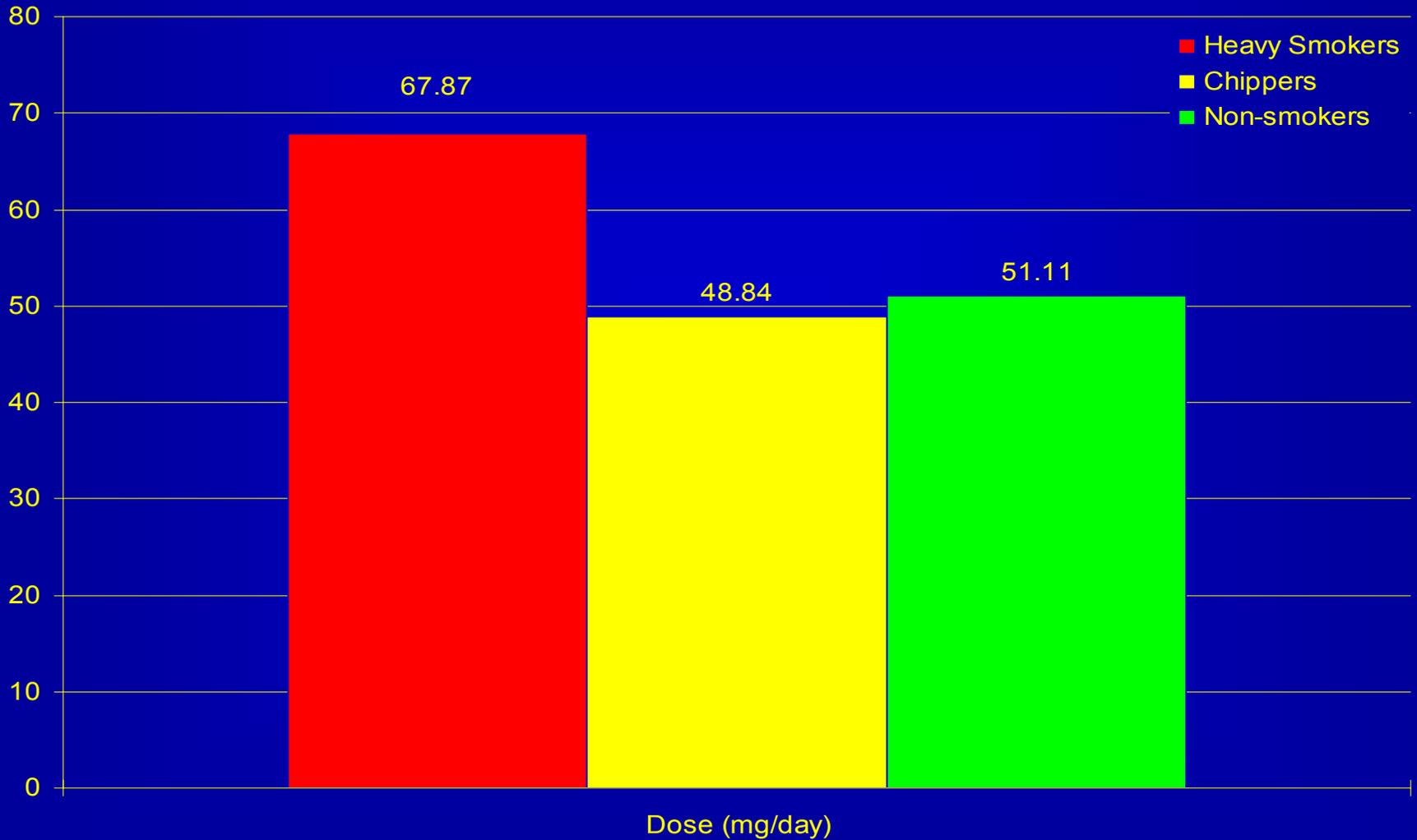
\*\*p<.05, \*p<.10

# Cocaine and Opiate TES by Group



\*p<.01

# Daily Methadone Dose by Group



# Relationship of Methadone Dose, Smoking Status, and Opiate TES

Variable Entered	$\Delta R^2$	$\Delta F$	Significance
Methadone Dose	.12	4.03 (df = 1,29)	n.s.
Smoking Status	.36	9.49 (df = 2,27)	p<.01

Final Model:  $F(3,27) = 8.46, p<.001$

# Relationship of Methadone Dose, Smoking Status, and Cocaine TES

Variable Entered	$\Delta R^2$	$\Delta F$	Significance
Methadone Dose	.04	1.22 (df = 1,29)	n.s.
Smoking Status	.22	4.06 (df = 2,27)	$p < .05$

Final Model:  $F(3,27) = 3.20, p < .05$

# Conclusions

- **Tobacco “chipping” extends to methadone maintained tobacco smokers**
- **Ordered relationship between nicotine, cocaine, and heroin use**
- **Association appears to be stronger than the relationship between methadone dose and illicit drug use**

# Smoking Cessation Treatment at Inpatient and Residential Drug Rehabilitation Programs: Research over the Past Decade

- **Types of Smoking Cessation Programs**
- **Smoking Abstinence Quit Rates**
- **Effects on Drug and Alcohol Use**
- **Retention in Drug Rehabilitation**



# Joseph and colleagues, 1993

- 3 group lectures and hand-out material with no nicotine replacement (n=154) vs standard care (n=160), at 21-day residential rehabilitation program.
- Smoking abstinence - Intervention Group  
Quit smoking for at least 1 week: 19% (\* vs 3%)  
10-16 mo. post-discharge: 10% (smoke cess) vs 3% (control)
- Self reported drug & alcohol improvement  
10-16 mo. post-discharge: 55% (smoke cess) vs 62% (control)
- Rehabilitation retention, 1 week post enrollment:  
91% (smoking cess) vs 91% (control)\*

# Hurt and colleagues, 1994

- 10 group counseling sessions with optional nicotine gum (n=51) vs standard care (n=50), at Mayo Clinic inpatient drug and alcohol rehabilitation program (postdischarge phone/mailings).
- Smoking abstinence  
End of Treatment: 22% (smoke cess) vs 10% (control)  
52 week postdischarge: 12% (smoke cess) vs 0% (control)\*
- Drug & Alcohol abstinence - Both Groups  
52 week postdischarge: 67% (smoking cess.) vs 66% (control)
- Rehabilitation retention, length of stay:  
24 days (smoking cess) vs 28 days (control)

# Bobo and colleagues, 1998

- Individual smoking cessation counseling (n=240: 6 sites) vs. standard care (n=246: 6 sites) prior to discharge from residential alcohol and drug rehabilitation programs and at 8, 12 and 16 week post discharge via telephone.
- Smoking Abstinence
  - 4 wk post discharge: 3% (smoking cessation) vs 2% (control)
  - 26 wk post discharge: 8% (smoking cessation) vs 4% (control)
- Drug Abstinence
  - 4 wk post discharge: 19% (smoking cessation) vs 21% (control)
  - 26 wk post discharge: 34% (smoking cessation) vs 35% (control)
- Alcohol Abstinence
  - 4 wk post discharge: 74% (smoking cessation) vs 72% (control)

# Burling and colleagues, 2001

- Individual counseling with nicotine patch following a nicotine fade (n=50) vs standard care (n=50), VA residential alcohol and drug rehabilitation program (treatment after minimum of 30 days in program).
- Smoking abstinence
  - 4 wk post-quit: 40% (smoke cess) vs 2% (control)
  - 12 & 26 wk post-quit: 18% (smoke cess) vs 11% (control)
- Drug & alcohol abstinence
  - 4 week post-quit: 77% (smoke cess) vs 61% (control)
  - 12 week post-quit: 67% (smoke cess) vs 63% (control)
  - 26 week post-quit: 67% (smoke cess) vs 67% control)
- Smoking cessation retention, full 9 wk Tx: 45%

# Summary of Previous Research

- Stopping smoking during drug or alcohol rehabilitation: no negative impact on treatment of drug and alcohol dependence
- Moderate success in quitting smoking is obtained, better with nicotine replacement therapy
- Evidence for improved rehabilitation retention, and reduced alcohol drinking

# Smoking Cessation Study: NIDA-CTN-0009

- Protocol Development
  - Concept Submission and Protocol Development by Committee
  - Team of Scientists, Clinic Directors, NIDA
- Communications
- Design Factors
  - Clinic and Clients: Feasibility and Interest
  - Medications
  - Counseling Platform
  - Site Logistics and Staffing needs

# Smoking Cessation Study: Study Intervention

- Smoking Cessation State-of-the-Art
  - Counseling: Mood Management and Cognitive Behavioral Treatment to Prevent Smoking Relapse
  - Medication: NicoDerm CQ

# Smoking Cessation Study: Pharmacotherapy

- Study Design Issue: Selection of nicotine patch therapy
  - Drug availability: GlaxoSmithKline - NicoDerm CQ
  - OTC medication: Good safety profile, no need for MD oversight, “real world” availability.
  - Efficacy: Equal with Zyban in standard smoking cessation efficacy trials. Most effective when combined with counseling
  - Program Integration: Already offered in some drug rehabilitation settings (MMTP, alcoholism TX)

# Smoking Cessation Study: Counseling Program

- Counseling Platform:
  - Mood Management and Cognitive Behavioral Smoking Cessation Program (Hall, Muñoz, Norman, at UCSF).
  - Group Counseling: 2 pre-quit week, 2 post-quit week, weekly for treatment weeks 2-6
  - Staggered Start: Smoking Cessation Treatment Initiated every 4th week
  - CTP smoking cessation counselors must be non-smokers
  - Counselor supervision and monthly QA ratings

# Smoking Cessation Study: Design Elements

- Study Design Issue: Control Subjects
  - Ethics: Desire of clinics to offer smoking cessation to all study participants
  - Retention: Adequate outcome data from non-treatment, control group
  - Solution: Deferred smoking cessation for control group (eligibility = expected level of study compliance)
- Study Design Issue: Open label medication
  - Ethics: No placebo group = all study participants receive full treatment intervention.

# Smoking Cessation Study: Protocol Development

- Study Design: 9 wk treatment trial (1 wk + 8 wk)
  - All subjects continue standard outpatient substance abuse rehabilitation
  - Smoking cessation treatment vs control group:
    - Group 1: Smoking Cessation Counseling and NicoDerm patch
    - Group 2: No Smoking Cessation Treatment (26 wk deferred)
  - One study protocol applied in two settings: Drug Free Outpatient or MMTP/LAAM Clinics (72 patients/clinic)
  - Smoking prevalence, Client interest, Drug Use and Smoking Assessments, Drug Rehabilitation Retention
  - Assessment Schedule: 1 x wk, Follow-up at 13 wk and 26 wk post-quit date

# Smoking Cessation Study: Timeline and Longterm Goals

- Protocol Development: 2 yr
- Protocol Implementation: 12 sites across the country
  - Study Initiation: June, 2002
  - Enrollment Completion: August, 2003
  - Study Completion: February, 2004
- Legacy: Participating clinics establish smoking cessation counseling programs. Assistance with medication procurement.